

**RECORD OF TELEPHONE CONVERSATION**

Submission Type: BLA Submission ID: 125428/0 Office: OVRR

Product: Hepatitis B Vaccine (Recombinant)

Applicant: Dynavax Technologies Corporation

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Communication Category(s): Information Request

Author: KATHERINE BERKHOUSEN

Email/telecon Summary: Secure email IR for chemistry, antigen, potency testing from  
DMPQ/ LACBRP

FDA Participants: K. Berkhausen Non-FDA Participants: E. Alambra (Dynavax)

Telecon Body:  
Dear Elaine,

We have the following requests for information. We realize that your response to some  
of our requests may take some time. We therefore ask that your response to provide us  
with the requested 'documents' not wait; and that you submit these documents as soon as  
you have the information available. -----Kind regards, Katherine

1. Please submit the following documents:
  - a. SOP A005: Determination of HBsAg (b) (4) cited in QS 491
  - b. SOP QC006: Method for (b) (4)
  - c. SOP QC 008: Method for (b) (4)
  - d. VAL-QC 113/089: Validation Protocol/Plan for In vivo potency
  - e. SOP A012: Validation of Methods and (b) (4) Method, Validation /Plan  
and Report for comparison of (b) (4) assay kit
  - f. QX011: Method Validation and Protocol/Plan for comparison of  
(b) (4) assay kit
  - g. VAL-QC 118: Validation Protocol/Plan I for (b) (4) for identity and  
(b) (4)

- h. SOP A116-3: Validation Protocol/Plan for QS 784, QS720, QS677, QS491
  - i. SOP QC 128-03: Determination of (b) (4) of HBsAg DS and its Validation Plan and Report (VAL QC209A/QC 128-01-R)
  - j. VAL-248A/QC12803-P: HBsAg Stability study by (b) (4) - the Validation plan and report
  - k. SOP 237: Relative potency determination for In Vivo potency assay.
  - l. Method Validation report, Validation Protocol/Plan and Immuno Assay Manual for QC089-5 ((b) (4) Assay)
  - m. AD-2008-07: Analytical Development Report for (b) (4) for In-process HBsAg Drug substance
  - n. SOP QTM-000039: (b) (4) of 1018 ISS Adjuvant by (b) (4)
  - o. SOP QTM-000053 (or MF/QTM/053): (b) (4) of 1018 ISS Adjuvant by (b) (4)
  - p. SOP QTM-000051: (b) (4) Analysis for 1018 ISS Adjuvant
  - q. SOP QTM-000076 (or MF/QTM/076): (b) (4) Analysis of 1018 ISS Adjuvant (for impurity analysis)
  - r. SOP MF/SOP/088: Determination of % Purity and Impurities of Oligonucleotides by (b) (4) .
  - s. SOP QTM-000074: Determination of (b) (4) of AGU in In-Process & API Samples by (b) (4)
2. We have the following comments regarding validation of the method entitled (b) (4) for In-process HBsAg Drug substance (Module 3.2.S.4.3):

(b) (4)



(b) (4)

(b) (4)

(b) (4)

(b) (4)

11. We have the following comments regarding validation of the method entitled *Determination of HBsAg Protein Concentration in Heplisav Drug Product by the (b) (4)* (Module 3.2.P.4.3):
- a. Please identify which of the results included in Table 2 of the validation report (Document # VAL-DE A090-4-R) were performed at the Dynavax Berkeley laboratory and which ones were performed at the Dynavax Europe laboratory.

- b. Section 7.2 (Specificity) of the validation report (Document # VAL-DE A090-4-R) states, "Dynavax Berkeley qualification report QUAL-Q116C-R demonstrates that (b) (4)"  
(b) (4)  
Provide the qualification report QUAL-Q116C-R.
- c. Provide results showing Specificity, Intermediate Precision and Reproducibility (Inter-laboratory Precision) using (b) (4) concentrations over the Range of the assay, (b) (4)
- d. How are the Expected Concentrations reported in section 7.3.2 of the validation report (Document # VAL-DE A090-4-R) determined? Have you used the same assay method or a different method?
- e. We do not agree that Accuracy of an assay can be inferred automatically once linearity, precision and specificity are established. Provide data to show Accuracy over the Range of the assay. At the minimum Accuracy should be studied at three concentration levels, the target concentration, and the lowest and the highest concentrations of the assay Range.
12. We have the following comments regarding SOP QC109: *Determination of 1018 ISS Adjuvant Identity and Concentration determination by (b) (4) for ISS* and validation of the method (Module 3.2.P.4.3):
- a. How is the extinction coefficient cited in Section 3.2.1 (p. 3) of the SOP QC109-02 determined?
- b. Provide description of Sample 1 and Sample 2 used for System Suitability study in the method validation report, Document No. VAL-Q139C-R.
- c. How do the concentrations of (b) (4) used in the Specificity study compare to those in the formulated product?
- d. What are the (b) (4) of the diluents (b) (4)  
(b) (4)  
in the Specificity study? Did the diluents contribute to (b) (4) of the analyte, when the analytes are diluted with them?
- e. We do not agree that Accuracy of an assay can be inferred automatically once linearity, precision and specificity are established. Provide data to show Accuracy over the Range of the assay (b) (4). At the minimum Accuracy should be studied at three concentration levels, the target

concentration, and the lowest and the highest concentrations of the assay  
Range.